Joint Bayer CropScience and Valent U.S.A. Corporation

Response to the Clothianidin Petition

Comments to Docket # EPA-HQ-OPP-2012-0334

September 24, 2012

Attachment 1 – Technical Response

A. Introduction

Four environmental and consumer organizations (Pesticide Action Network of North America, Center for Food Safety, International Center for Technology Assessment, and Beyond Pesticides) as well as 27 beekeepers and beekeeping associations submitted a petition (Regulations.gov.; EPA-HQ-OPP-2012-0334-0002) to EPA, dated March 20, 2012, requesting the suspension of registrations for the insecticide clothianidin based on alleged imminent harm to pollinators, as well as initiation of special review and cancellation proceedings, and issuance of a stop sale, use and removal order. In a letter of July 17, 2012 (Regulations.gov.; EPA-HQ-OPP-2012-0334-0006), the U.S. Environmental Protection Agency (EPA) explained their decision to deny the imminent harm portion of the petition and indicated that they would address the other portions of the petition after requesting public comments. The Agency also published a technical explanation of the data that supports their decision to deny the request for suspension in the petition. This explanation is given in the Environmental Fate and Effects Division (EFED) Technical Support Document (TSD) (Regulations.gov.; EPA-HQ-OPP-2012-0334-0012).

Bayer CropScience LP ("Bayer") and Valent U.S.A. Corporation ("Valent") previously submitted preliminary comments (Regulations.gov; EPA-HQ-OPP-2012-0334-0008) regarding this petition particularly addressing the allegations of imminent harm ("Preliminary Comments"). The EPA legal and technical partial response to the petition, as well as the comments from Bayer and Valent, clearly show that the petition fails to justify the requested actions. By categorizing the primary concerns raised in the petition and responding to each, this document provides additional clarifying technical information showing that many of the allegations and interpretations given in the petition are misleading or simply incorrect.

B. Nature of Incidents

The petitioners allege that clothianidin has been observed to cause the type of bee kills attributed to Colony Collapse Disorder (CCD) and cite incident data in the North America and Europe to support their allegation. However, the acute exposure incidents cited for neonicotinoid-based seed treatment products are not consistent with the characteristics of CCD.[1,2] As explained in Bayer's and Valent's Preliminary Comments, the scientific data does not support any relationship between these alleged limited acute exposure incidents resulting in the death of individual bees, and the allegations relating to colony- and population-level declines in bee populations that form the basis of the petition. Furthermore, as noted in the petition, neonicotinoids and clothianidin in particular are used annually on millions of acres in North America – most frequently as neonicotinoid-treated seeds. This use on vast acreage has resulted in very few acute exposure incidents, further indicating that acute risk to neonicotinoids is not common and is clearly not a factor in long-term honey bee declines.[3]

Foliar clothianidin insecticides have also been applied on many agricultural crops on hundreds of thousands of acres. Their use patterns range from post-bloom use on almonds for increasing stink bug problems, to soil and foliar uses in crops such as sweet potatoes. Again, very few incidents of harm to individual foraging bees have been reported following foliar applications of clothianidin. Investigations of these incidents concluded that applications were made to fields adjacent to bee hives, and in which bees were actively foraging on a blooming crop on a daily basis; some foraging bees died due to acute toxicity from the exposure. Unfortunately, in these cases, the product was not used in accordance with label directions.

In several European countries (e.g. UK, Germany, The Netherlands), surveillance systems are in place to record and investigate pesticide-related incidents with bees. The statistics show that instances of bee damage caused by acute pesticide exposure incidents are continuously trending downward, and are on a relatively low level.[4-6] Among these cases, incidents with neonicotinoid products are rare and mostly caused by a failure to follow label directions for use, or to specific issues related to the particular seed treatment or sowing equipment used in those countries.

Some beekeepers in Ontario, Canada, recently (Spring 2012) noticed losses of honey bees coinciding with the timing of corn planting. Preliminary information indicates that pesticides on treated seeds may have been a contributing factor to some of the losses. However, clothianidin-treated corn and canola seed has been planted extensively in Ontario and western Canada without incident since 2004. Government agencies are investigating the reasons for the losses and plan to issue a report of the findings and conclusions.

C. European Perspective

The petition makes reference numerous times to European events regarding bee health and neonicotinoids. The OPERA Research Center in Europe recently published a report titled "Bee-good Bee Health in Europe – Facts and Figures; *Compendium of the Latest Information on Bee Health in Europe.*"[7,8] The following excerpt from the Executive Summary of that report summarizes the current situation regarding bee health in Europe, and demonstrates the inaccuracy of the petitioners' allegations regarding the experiences and regulatory approach in Europe:

> *"Decline of honey bee colonies have been reported mainly in central Europe, but the situation in not universal, since in Mediterranean countries increases have been observed over the past decades. The media frequently reports alarming numbers of colony losses, but in many cases the reasons for decline - which are typically complex and multifactorial in effect - are poorly investigated and the information given on overwintering colony losses is often misleading. Typically the implication is that decline in honey bee colonies is affecting all bee species, when the causes and effects are more often specifically related to the keeping of hived bees.*

Whilst overwintering colony losses have increased by trend in the last decade, these are not significantly different for single years registered in the past. When high colony losses are reported, most reports from Europe are about overwintering losses caused by the Varroa spp. mites, often linked with secondary infections by viruses and losses caused by Nosema spp.

The outcome of the multifactorial monitoring projects reported so far seems to suggest that the parasitic pest mite Varroa spp., which can be found in almost every apiary in Europe, is the main causative factor involved in honeybee colony weakening in Europe.

Other diseases like Nosema spp., virus infections, or foulbrood, may also damage colonies during spring and summer. Due to the lack of veterinary treatments, parasites and diseases commonly affect these bee populations. Furthermore, it is also expected that diseases which are not currently present in Europe, such as the small hive beetle or the Trolilaelaps spp. mite may appear and spread. The efficacy of current treatment options, where they are used, varies based on beekeeping practices, climatic conditions and different seasonality.

Colony Collapse Disorder (CCD) as described in USA has not been observed in Europe.

Controlling bee pests and diseases is seen as the essential factor for successful beekeeping over the years. Some countries made important efforts to implement specialized training programs for the recognition of diseases; in others this skill is gravely underdeveloped with beekeepers.

Additionally, as beekeeping techniques, cultural traditions and climatic conditions vary around Europe, greater attention should be paid from the policy side to the development and implementation of good beekeeping guidelines. New beekeeping techniques and improved knowledge have resulted in improved bee health and higher quality and quantity of honey yields.

Pesticides are listed by many authors as a potentially contributing factor to honeybee colony losses, but there are only few investigations that claim to have found concrete evidence for a key role of pesticides. Reported pesticide incidents typically lead to a varying degree of damage on the colony, but rarely the loss of damaged colonies. The most frequent cause of pesticide-related incidents is the misuse of products and ignorance of label statements by farmers, combined with a poor communication with beekeepers, or disregard by beekeepers for good practices. Single events of poisoning with pesticides have thus been reported in many countries.

The role of multiple pesticide residues in sub lethal amounts, or the impact of combinatory and synergistic effects on bee health, evaluated also in the multi-factorial studies, requires further investigation. However, such research does not preclude the need to strictly respect *and adhere to the approved conditions of use for pesticides, which are designed to avoid exposure.*

In discussing the pesticide exposure of bees, it is essential to consider if bees will be physically exposed to a product in the course of its use, based on the details of the product and its pattern of use. In some cases exposure of bees is not possible, and in case it is, a second consideration is the attractiveness of the crop plant. These are elements considered in current risk assessment schemes and as a consequence, the evaluation of incident reports, established in eight European countries, show that the number of pesticide-related bee incidents has generally declined for the past decades in the monitored countries.

Several post-registration monitoring studies have also been performed in countries across Europe to assess the impact of certain pesticides on bees in their predefined use conditions. Most of these were focused neonicotinoid substances. None of the pesticide-related bee monitoring in real-life conditions of use have, so far, found a clear connection between bee colony mortality as a general phenomenon and the exposure of bees to the pesticides. These have proved that the mitigation or stewardship measures decided at the approval of the respective products have been effective if complied with.

Multi factorial studies are the most dedicated approach as they are designed to quantify the relative contribution of each of the parameters monitored to any losses. Researchers agree that even if infestation with Varroa spp. is one of the major factors, a multi-factorial origin of the observed colony losses is most likely to be the cause. Other factors include a multitude of diseases and parasites, hive management and beekeeping practices, climatic factors, queen health issues, nutritional problems, loss of genetic diversity, and environmental factors such as the structure of modern agricultural landscapes."

This extensive report concludes that the chronic decline of honeybees in the European Zone is, as is the case for North America, multi-factorial in nature, and that there is no evidence that this decline is pesticide-driven, let alone caused by neonicotinoids or clothianidin in particular.

There is widespread use of neonicotinoids as seed treatments in European countries. In a few European countries (France, Germany, Italy, Slovenia), selected neonicotinoid seed treatment products have been suspended. In most cases, these suspensions include limited uses in specific crops while other neonicotinoid uses are still approved in these countries. In no country, is there a complete ban of neonicotinoid products. Existing suspensions were put in place either as a precautionary measure or as a consequence of incidents for which there are still investigations ongoing by the authorities. It should be noted for instance that France saw no improvement in bee decline after the suspension of seed treatment products that had been alleged to be involved in colony losses.

In many countries in Europe monitoring projects are established to survey colony mortality and to investigate causative factors behind colony losses. Some of them involve quite extensive observations, as, for instance, the German Bee Monitoring[3b] which is ongoing since 2004 where more than 1,000 hives distributed all over the country are monitored. In none of these monitoring projects has any correlation been found between in-hive residues of neonicotinoids or exposure to neonicotinoid-treated crops and colony mortality.

In sum, contrary to the claims of the petition, bee decline in Europe has not been linked to the use of pesticides in general or neonicotinoids in particular. In fact, bees are not declining in all of Europe with some parts showing bee increases over the last few decades. Therefore, addressing decline of managed bees in Europe, as in North America, will require a multi-factorial approach looking at all potential contributors.

D. Potential Relationships Between Bee Declines and Pathogens, Parasites, Bee Nutrition, Pesticides, Bee Management Practices and other Factors

The petition acknowledges that:

> "*research has linked recent declines of honey bee colonies and other native bee pollinators to a constellation of stress factors, including pesticides, pathogens and nutrition*".

Despite this statement, the petition goes on to focus on clothianidin and other neonicotinoids and asserts without support that they are primarily responsible for bee declines and CCD. However, reputable scientists, regulatory agencies, beekeepers and others agree that the declining health of managed bee colonies seen in recent years is likely a result of many factors[4,5,9-14], and attention has turned increasingly to the parasitic *Varroa* mites and associated pathogens as the principal causes. The University of Georgia recently confirmed this when it reported on the Managed Pollinator CAP (Coordinated Agricultural Project) (http://www.beeccdcap.uga.edu/) in September 2011, indicating that any concern around the newer neonicotinoid pesticides was misplaced. Since 2008, the University of Georgia has led the $4.1 million USDA Managed Pollinator CAP program, a 17-member consortium of university and federal bee labs "dedicated to the reversal of honey bee decline." Keith Delaplane, National Director for the CAP program, has stated,

> *"If our CAP has reached any one overarching conclusion, it is that 'bee decline' is a huge issue and not easily reducible to one or a few 'causes.' It is instead a web of causation, and the answer will involve not only good bee husbandry, but revisions to our land use and pest control habits."*[9]

Furthermore, Delaplane goes on to explain that the CAP program has shown that the Varroa mite, present in the USA since 1987, is a vector of many viruses, among them the Israeli Acute Paralysis Virus (IAPV), one of the viruses implicated in bee colony deaths. Research has shown that IAPV levels go up as Varroa levels go up,

> *"which turns the spotlight toward Varroa as the underlying problem."*[9]

Similarly, the most recent CCD Progress Report from the USDA CCD Steering Committee[13] stated the following:

> *"although a number of factors have been associated with CCD and pollinator declines in general, no single factor or specific combination of factors has been identified as a 'cause'. Factors associated with declines include disease/parasites, nutrition, pesticides, bee management practices, habitat fragmentation, and agricultural practices. Reducing the incidence of CCD and pollinator declines will likely require managing multiple factors simultaneously."*

While the petition and an accompanying report point selectively to studies that have shown effects on bees under artificial study conditions frequently using exaggerated neonicotinoid exposure levels, bee researchers and other scientists who have evaluated the data relative to neonicotinoids and bee decline do not agree with the allegations made in the petition. Most scientists and regulators have concluded that, while lethal and sublethal effects of neonicotinoid insecticides on bees have been produced in laboratory studies or other tests conducted under artificial exposure conditions, no adverse effects at colony level have been observed in field studies with field-realistic exposures.[14, 31-35] These conclusions mirror those of EPA that the available data do not indicate that nitroguanidine neonicotinoids, including clothianidin, are causing substantial adverse effects on bees or that there is a connection between CCD and the neonicotinoid insecticides.

E. Use and Persistence of Clothianidin

The neonicotinoids are a class of insecticides that are composed of two primary sub-classes; the nitroguanidines (imidacloprid, clothianidin, thiamethoxam, nitenpyram and dinotefuran) and the cyano-amidines (acetamiprid and thiacloprid). The nitroguanidines are systemic insecticides with residual soil activity which allows them to be used as seed, soil and foliar treatments. The cyano-amidines have little soil residual activity and, as a result, are used primarily as foliar treatments. The nitroguanidines are used extensively as seed treatments on numerous agronomic crops such as corn, soybeans, canola, and others, plus there are numerous uses of these compounds as soil and foliar treatments on agricultural crops. The use of the neonicotinoids as seed treatments on many acres in the USA offers a more environmentally responsible means of protection of seeds and early seedlings since there are far fewer bee kills now than prior to the introduction of the neonicotinoids.[14]

As noted above, the nitroguanidines exhibit longer soil residual activity, which makes them effective as seed and soil treatments. The petition raises concerns about this residual soil activity suggesting that it would eventually lead to accumulation of residues in environment. The implication is that this would lead to higher residues in bee relevant matrices such as pollen and nectar. However, the scientific data demonstrate that there is no accumulation of residues of nitroguanidine insecticides in nectar and pollen even from repeated applications year after year.

Results recently generated for the California Department of Pesticide Regulation confirmed these conclusions.[14] Furthermore, the results from an extensive nationwide survey of bees, pollen and wax residues demonstrated that systemic pesticides including systemic neonicotinoids were found relatively infrequently, and clothianidin was not found in any samples.[15]

F. Non-Target Organisms

The petitioners quote a passage from EPA's original fact sheet for the conditional registration of clothianidin:

> *Clothianidin is expected to present acute and/or chronic toxicity risk to endangered/ threatened birds and mammals via possible ingestion of treated corn and canola seeds. Endangered/threatened non-target insects may be impacted via residue laden pollen and nectar. The potential use sites cover the entire U.S. because corn is grown in almost all U.S. states.*

Petition at 24 (quoting EPA Clothianidin Pesticide Fact Sheet at 16 (May 30, 2003)). Among other things, however, they fail to acknowledge the subsequent paragraph in which EPA goes on to explain how any such potential ecological concerns have been addressed and mitigated through restrictions on how registered products can be used.

> *To address ecological concerns, labeling will be required that mandates treated seed bags be printed with advisory language regarding hazards to wildlife and will include specific instructions to cover or collect clothianidin treated seeds that are spilled during loading.*

EPA Clothianidin Pesticide Fact Sheet at 16 (May 30, 2003). Current EFED modeling assumptions provide that only 1% of the active ingredient still available on the seeds can be foraged if the seed is covered during drilling. The conclusion stated by EPA is based on a scientific evaluation of the potential for exposure to wild birds and mammals.

As a consequence, all product labels for seed treatment products containing clothianidin require statements to be included on all bags of treated seed such as:

> *This compound is toxic to birds and mammals. Treated seeds exposed on soil surface may be hazardous to birds and mammals. Cover or collect treated seeds spilled during loading.*

In other words, the EPA statements regarding "possible" concerns highlighted by the petitioners are incomplete, and do not necessarily apply to the actual use of clothiandin products as registered by EPA. The Agency and registrants have established mitigation and label language to protect birds and mammals from seeds treated with clothianidin.

G. Clothianidin and Colony Collapse Disorder

The petition fails to fully acknowledge the distinction between Colony Collapse Disorder (CCD) and acute effects on bees. The characteristics of CCD according to USDA, as described by vanEngelsdorp et al.[1], include (1) the apparent rapid loss of adult worker bees from affected colonies as evidenced by weak or dead colonies with excess brood populations relative to adult bee populations; (2) the noticeable lack of dead worker bees both within and surrounding the hive; and (3) the delayed invasion of hive pests (e.g., small hive beetles and wax moths) and kleptoparasitism (stealing food) from neighboring honey bee colonies.

As noted in this description, colonies suffering from CCD show a noticeable lack of dead worker bees both within and surrounding the hive. In contrast, when bees are accidently exposed to high levels of an insecticide, an acute poisoning can occur that results in the presence of dead worker bees outside the hive. While this may result in the loss of worker bees it rarely results in the loss of an entire colony. The neonicotinoids, (as with most other insecticides), are acutely toxic to adult bees exposed to sufficient levels and, if an acute exposure incident occurs, can elicit the same symptomology as that noted for generalized acute poisoning, but NOT those typically associated with CCD.

H. Bee Exposure to Neonicotinoids/Clothianidin

When considering an alleged potential link between neonicotinoids and CCD it is important to remember that elevated residues of clothianidin and other nitroguanidine neonicotinoids have not been found in any colonies that have suffered from CCD, and that the occurrence of CCD is not higher in regions of the county where clothianidin and other nitroguanidine neonicotinoids are most frequently used.[1, 16,17]

There are two primary means of potential exposure of bees to neonicotinoids and clothianidin in particular: Direct exposure to airborne residues (from foliar sprays or abraded seed dust); or indirect exposure from ingestion of residues in pollen or nectar of plants grown from treated seeds or in treated soil. Acute exposures associated with spray applications or planting of treated seed could result in acute bee kills, but reports of such incidents are rare, especially in relationship to the large number of acres treated each year. The colonies involved generally recover, and there is no reason to suspect that such incidents are a significant factor in decline of managed bee populations. Furthermore, an evaluation of the available residue data indicates that neonicotinoid residues in pollen and nectar are generally significantly below the levels at which adverse effects occur. Actual measured residues of neonicotinoids found in pollen and nectar of treated plants are generally in the range of 1-3 ppb (rarely above 5 ppb).[14] In fact, in what the petition calls "the most extensive North American survey of pesticide residues in managed honey bee colonies to date in 23 states and one Canadian province …" looking at pesticide residues in bees, pollen, and wax, systemic pesticides, including the systemic nitroguanidine neonicotinoids, were detected relatively infrequently. Clothianidin was not detected in any of the samples. Where residue analyses were conducted on colonies which eventually succumbed to CCD, elevated levels of neonicotinoids were not found[1,16,17]. All of these results demonstrate that the neonicotinoid insecticides are not a significant contributing factor to overall bee decline or CCD.

The petition makes much of reports from Italy of the potential for neonicotinoid residue to be present in the guttation water of plants grown from seeds treated with neonicotinoids. However, most bee experts agree that guttation water is not a significant source of water for bees and consequently not a significant risk to pollinators. A compendium of the latest information on bee health in Europe from the OPERA Research Center discusses the potential and significance of pesticide residues in guttation water of plants grown from seeds treated with systemic insecticides such as neonicotinoids:[7]

> *"The exposure of bees via uptake of guttation water containing residues of systemic insecticides such as neonicotinoids have been discussed and highlighted by Italian researchers. The level of residues in guttation droplets depends on different elements; the potential risk from different crops varies depending on the relative intensity and frequency of guttation events, crops, and the amount of active substance per seed as well as other factors. Guttation exposure can be very easily avoided by beekeepers through the provision of clean water in the vicinity of the hives. Recent research data (Pistorius et al., in press[20]; Keppler et al., 2010[21]) have demonstrated the issue of guttation is of comparably low importance compared to intoxications by spray applications and indicate that in certain circumstances only small numbers of bees of a hive may be intoxicated, even if colonies are placed directly next to crops. The risk is likely to decrease rapidly within a few meters distance of the colonies to treated crops. The data indicate damage to colonies in worst case scenarios are on a low level. Effects on colony strength, brood development and overwintering have not been observed. Also, in incident reporting schemes e.g. in Germany (Pistorius, pers. comm.) no apparent poisoning incidents linked with guttation were reported by beekeepers or ascertained during subsequent investigation.*[7]

The petition further alleges that the decline of honey bees in the United States coincides with the introduction of neonicotinoids especially clothianidin in this country. However, as noted by EPA, vanEngelsdorp and Meixner[21] in their historical account of bee decline in the United States, show that there has been a steady decline in managed honeybee colonies over the past 60 years while neonicotinoids have been on the market for about 20 years. This decline is likely the result of many factors including *Varroa* mites which were introduced to the USA in 1987 and are now likely the number one bee management problem. Other contributors to bee decline likely include changes in agricultural and bee management practices as well as diseases and other factors.

I. Synergistic Effects of Neonicotinoids and Other Pesticides as Well as Pathogens

The petition further speculates that the toxicity of the neonicotinoid insecticides is synergistically enhanced by certain fungicides. However, this assertion is incorrect and is based on a poor understanding of the differences between neonicotinoid insecticides as well as the research results. The petition cites only the data from Iwasa, et al.[22] which did show synergism of two cyano-amidine neonicotinoids (acetamiprid and thiacloprid) with two DMI fungicides, but show no synergism of imidacloprid, a nitroguanidine neonicotinoid with these fungicides. As noted by EPA there is no reason to anticipate synergistic activity between fungicides and any of the nitroguanidine neonicotinoids (including clothianidin) based on their resistance to degradation by honey bee P450 enzymes. Therefore, synergism of clothianidin with fungicides is not an issue of concern for honey bees. In addition, the increased toxicity of the cyano-amidine neonicotinoids in combination with the fungicides was seen only in the laboratory with no such increase seen under field conditions. Therefore, under real-world field use conditions, the combined use of any neonicotinoids with DMI fungicides is not expected to result in synergistic effects. In fact, there is no data showing synergistic effects of neonicotinoid insecticides and other pesticides under field conditions.

The petition also gave an incomplete report on the studies looking at the impact of neonicotinoid exposure and the common hive parasite *Nosema*. Pettis et al. 2012[26] did report higher *Nosema* infection levels developed in young adult bees emerging in a laboratory incubator from brood frames taken from hives in the field that had been fed imidacloprid-spiked food. However, these authors did not find the same to be true for the source hives in the field. There was no difference in *Nosema* infection levels between hives fed imidacloprid-spiked food and those fed a pesticide-free diet. Alaux *et al.* 2009[23], while reporting a higher mortality rate for honeybees exposed under laboratory conditions simultaneously to imidacloprid and *Nosema* infestation, found that exposure to imidacloprid actually reduced the level of *Nosema* infections. This is exactly the opposite of the results of Pettis et al.'s laboratory study. A third study from the Bee Institute of Celle/Germany, which was conducted under more realistic exposure conditions, did not find interactions between sublethal exposure to imidacloprid and a challenge with *Nosema* infestation (Wehling *et al.* 2006[24], 2009[25]). When all of the available data on the interaction of neonicotinoids and *Nosema* are considered, the claims of the petitioners are not supported. There appears to be as much, if not more, empirical evidence suggesting neonicotinoids inhibit *Nosema* infections in honey bees as there is evidence for them increasing these infections. It is also worth noting that, although early research suggested *Nosema* may play a key role in the occurrence of colony collapse disorder, subsequent research "*has not found Nosema to be a predictor of CCD or general colony loss, and the broad distribution of Nosema in apparently strong colonies contradicts a unifying role for these pathogens in CCD*" (quotation from Cornan et al. 2012[27]). Thus, even if neonicotinoids did increase susceptibility of honey bees to *Nosema* infection, this still would not implicate them as contributing to CCD.

J. Sub-Lethal Effects of Neonicotinoids on Bees

A few recent studies on neonicotinoids have been accompanied by considerable media coverage with often highly exaggerated claims including going so far as to suggest that these products have been identified as the likely culprit in sharp worldwide declines in honey bee colonies. These media stories, while sensational, do not accurately reflect the science. These few recent sub-lethal studies looked at the impact of neonicotinoids on bee learning performance, orientation, foraging, social interaction, etc., mostly by performing experiments with individual bees at unrealistic exposure levels and/or in an artificial laboratory environment that does not relate to colony exposure in the field[14,18,31-35]. In contrast, researchers that review and weigh all relevant information continue to conclude that this is not the case, including in very recent publications (e.g. Delaplane, 2012[9]; Cresswell et al., 2012[29]; Szabo et al., 2012[30]; Blacquière et al. (2012)[31]. For example, Blacquiere, et al., summarized fifteen years of research on the risks of neonicotinoids to bees by looking at neonicotinoid residue levels in plants, bees and bee products as well as reported side-effects with special attention for sublethal effects. They then looked at the potential of using an existing risk assessment scheme designed for systemic compounds to evaluate neonicotinoids. They point out that:

> *"it is now accepted that the abundance of pollinators in the environment is influenced by multiple factors, including biotic ones like pathogens, parasites, availability of resources due to habitat fragmentation and loss; and abiotic ones like climate change and pollutants."*

Blacquiere, et al., conclude that the reported levels of neonicotinoids in nectar and pollen are below acute and chronic toxicity levels and the levels in bee-collected pollen, bees and bee products are low. These authors note that laboratory studies have shown many lethal and sublethal effects of neonicotinoids at artificially high exposure levels, but no effects have been observed in the field studies with field-realistic dosages.

As a further example, Cresswell, et al. [29] used Hill's epidemiological causality criteria to examine the evidence that the agricultural use of neonicotinoids is a cause of the recently observed decline in honey bees. They note that:

> *"the question of whether neonicotinoids cause bee population declines would be settled beyond reasonable doubt if realistically dosed honey bee colonies showed sufficient harm under field conditions."*

Based on their assessment of the available data they:

> *"conclude that dietary neonicotinoids cannot be implicated in honey bee declines."*

This conclusion is supported by field studies that have shown no adverse effects from neonicotinoids applied according to label directions.[14,18,31-35]

The actual measured amount of neonicotinoids in pollen and nectar of treated plants is typically in the range of 0-5 ppb. However, much of the research referenced in the petition exposed bees to levels orders of magnitude higher than this. Furthermore, these studies evaluated responses of individual bees under artificial laboratory conditions, rather than responses of whole colonies under field conditions. Studies that did include both laboratory and field experiments showed that under field-relevant conditions, neonicotinoids produced no significant adverse effects on the colonies.[18,26]

K. Significance of the Recent Krupke and Tapparo Studies regarding Planting of Neonicotinoid-treated Seeds

Two recent studies evaluated the potential exposure of honey bees to pesticides resulting from the use of neonicotinoid treated seeds. Krupke et al. (2012)[36] report the findings of a study on potential routes of exposures for honeybees to pesticides, especially to neonicotinoids, conducted in a corn-growing region in USA in 2010. The study was initiated in response to reports of acute bee kills at Indiana apiaries in the spring of 2010 which coincided with the corn planting period in the area.

While this study does not provide any fundamentally new evidence about honeybee exposure to neonicotinoid seed treatment products, it does highlight the need for best management practices during the planting of corn. The exposure levels reported in soil, pollen and nectar are largely consistent with previous research and were not high enough to represent a significant risk for honey bees. Higher concentrations found in waste talc collected from inside pneumatic equipment post-planting represent an intrinsic hazard to honey bees but actual exposure of bees to this material was not demonstrated and is preventable. In their field experiment, low exposure levels and no adverse effects were observed for bee colonies placed "in harm's way" around the perimeter of a field as it was being planted with treated corn seeds. Overall, the publication represents an interesting case study, as well as an opportunity for improved best management practices (along with equipment manufacturer and grower education), but it does not provide any significant new insights into exposure of honeybees to neonicotinoid insecticides.

Tapparo et al. (2012)[37] report on results of field experiments that measured emissions of particulate matter containing neonicotinoid insecticides from the sowing of dressed corn seeds and resulting potential exposure levels for honey bees. Various types of treated corn seeds were sown into a test field using two different types of pneumatic planters, and the amount of total particulate matter and active ingredient emitted into the air and deposited at various distances away from the planter or downwind edge of the field were determined. The experiments were run with and without downward deflectors mounted on planter's air exhaust outlet. Two different types of experiments were performed: "mobile sowing" and "static sowing". As part of the static sowing experiments, sugar syrup feeders and honey bee hives were placed so that bees would fly directly through the air exhaust of the planter, and become "powdered" with any emitted dust.

The authors conclude that if bees are flying over a field during the sowing of treated seed and approach they approach the emission cloud of the drilling machine they could intercept suspended particles in that cloud. These results demonstrate that when honey bees fly through the air exhaust of pneumatic corn planters they can become contaminated with abraded dust from insecticide-treated maize seeds and this can sometimes result in the death of individual bees. However, their research results and the available records of field incidents suggest that the problem of toxic exposure of bees to corn seed dust is limited in scope. Furthermore, the potential for such exposures can be addressed by improved seed coatings/lubricants, product stewardship measures and possibly planter design changes. This phenomenon has not been scientifically linked to, and there is no reason to suspect it is a cause of, colony collapse disorder or widespread honey bee colony declines.[38]

L. Conclusion

In short, the substantial body of research that has been established globally to date regarding root causation behind heightened overwintering losses of managed honey bee colonies (including CCD) clearly shows a complex, multifactorial interaction. In fact, the most common correlation appears to be some relationship between *Varroa* mites, viruses and potentially other pathogens such as *Nosema*.

The nitroguanidine class of neonicotinoids (such as imidacloprid and clothianidin) is acutely toxic to adult bees but a significant body of research does not support an association between their labeled use and chronic bee decline.

The characteristics of Colony Collapse Disorder (CCD) are not consistent with effects observed following acute bee exposure to neonicotinoids including clothianidin. Furthermore, the effects of neonicotinoid exposures on bee colonies vary in degree but seldom result in loss of the colonies. Despite widespread use of clothianidin globally there are few acute bee kills reported as noted by EPA and beekeepers in the US and national incident monitoring systems in Europe.

Actual measured residues of neonicotinoids in pollen and nectar of treated plants are generally less than 3 ppb, rarely above 5 ppb, well below any level of concern for pollinators. An extensive North American survey of pesticide residues in managed honey bee colonies looking at pesticide residues in bees, pollen and wax, showed that systemic pesticides, including the systemic nitroguanidine neonicotinoids, were detected relatively infrequently, with clothianidin in particular not detected in any samples.

A careful review of the extensive data regarding the effects of neonicotinoids on bees shows no indication of synergistic effects of nitroguanidine neonicotinoids with other pesticides whether in the laboratory or the field. Furthermore, none of the neonicotinoids showed any synergism with other pesticides or with pathogens under actual field use conditions. Therefore, synergism is not an issue of relevance for neonicotinoid insecticides.

Recent research indicating that neonicotinoids can produce sub-lethal effects on bees was generally conducted on individual bees under artificial laboratory conditions and at exaggerated exposure rates. Where simultaneous exposure was conducted under realistic field conditions and exposure levels no adverse effects were seen.

As noted by most scientists, regulatory agencies, beekeepers and others, the declining health of bee colonies seen in recent years is a result of many factors including parasitic Varroa mites and potentially *Nosema*, other pathogens, agricultural and bee management practices, bee nutrition, habitat fragmentation, and others. Although neonicotinoids including clothianidin are toxic to any individual bees that experience an acute exposure (as are many insecticides), exposure levels from the use of these products are generally below any level of concern for pollinators and not the cause of honey bee decline in the USA.

Finally, the use of neonicotinoids has been a significant advance in crop protection needed to feed an ever-growing global population. The effectiveness of clothianidin as a seed, soil and foliar treatment allows it to be a significant contributor to integrated pest management practices and to the increased sustainability of modern agriculture.

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